Reclassification of Nonthermal Shortwave Diathermy Devices

Industry Coalition Presentation

Richard A. Isenberg, MD

Vice President, Clinical and Regulatory Affairs

Regenesis Biomedical

Our Objective

Class II classification is appropriate:

- These devices all deliver the same dose to the patient
- RCTs provide strong evidence of effectiveness
- Risks to health are well identified and understood
- Special Controls can reasonably assure safety and effectiveness

Presentation Structure

1. Introduction and Regulatory Context
2. Technology and Dosimetry
3. Scientific Evidence
4. Risks, Mitigation and Proposed Special Controls
5. Conclusion

Industry Coalition

Industry Coalition ILX Devices

K Number	Year	Product	Manufacturer
K903675	1991	MRT SofPulse	Ivivi Health Sciences
K070541	2008	SofPulse 912-M10	
K070541	2008	SofPulse Roma^3	
K070541	2008	SofPulse Torino II	
K121388	2012	Zeobi	
K972093	1997	Provant Model 42	Regenesis Biomedical
K091791	2010	Provant System Model 4201	
K070931	2007	Model PMT850	ProMedTek
K091996	2009	Orthocor Knee System, Basic	Orthocor Medical
K092044	2009	Orthocor Knee System, XL	
K121702	2013	Orthocor, Active Device	

INDICATION

Adjunctive use in the palliative treatment of post-operative pain and edema in superficial soft tissue

Regulatory Context

Statutory Criteria for Reclassification to Class II

Special controls together with general controls provide reasonable assurance of safety and effectiveness of the device.

(Food, Drug, & Cosmetic Act)

1. Devices Deliver Uniform Dose

All Coalition devices deliver the same clinically meaningful dose to target tissues

Energy Density (μWs/cm^3)							
MRT	912-M10	Roma^3	Provant	PMT850	OrthoCor Knee	Torino II	Zeobi
0.14	0.13	0.12	0.13	0.14	0.13	0.13	0.13

2. Valid Scientific Evidence

Authors	Randomized Double-Blind Sham-Controlled	Surgery	Endpoints	P value
Hedén and Pilla (2008)	YES	Breast Augmentation	Pain, pill count	P<0.001
Rhode et al. (2010)	YES	Breast Reduction	Pain, pill count, exudate volume, IL-1β	P≤0.03
Rhode et al. (2012)	YES	TRAM-flap Reconstruction	Pain, pill count, exudate volume, IL-1β	P<0.02
Rawe et al. (2011)	YES	Breast Augmentation	Pain, pill count	P=0.002*
Kaplan and Weinstock (1968)	YES	Foot Surgery	Pain, swelling and erythema	P<0.01
Bentall and Eckstein (1975)	YES	Orchidopexy	Photodensitometry of photo of wound and wound circumference	P<0.05

* Pill count reduced in exposed group (P=0.07) but one exposed patient was outlier taking 33 pills. Excluding this patient P=0.002.

3. Risks Can Be Mitigated through Proposed Special Controls

Risk	IEEE C95.1	Electrical Safety	EMC	Preclinical Analysis	Labeling	Biocomp.	Clinical Information	QSR
Pacemaker Interference		✓	✓	✓	✓			✓
Tissue Necrosis and Burns	✓	✓		✓	✓		✓	✓
Wire Leads	✓	✓		✓	✓		✓	✓
Adverse Pregnancy Outcome	✓	✓			✓			✓
Risks to Children	✓	✓			✓			✓
Pain	✓				✓			✓
Skin Reaction	✓	✓			✓	✓		✓

Classification Panel History

In 1979:

- Limited information
  - Effectiveness data
  - Safety data

New Information Since 1979

- Valid scientific evidence
- Decades of collective safety experience in the market
- New Standards for design and performance

New Standards since 1979

Standard	Issued	Updated	Standardizes Controls for:
IEC 60601-2-3	1982	2012	Safety for Shortwave Therapy Medical Devices
IEC 60601-1	1988*	2005	General Safety of Medical Devices
IEC 60601-1-2	1993	2007	EMC for Medical Devices
ANSI/IEEE C95.1	1995	2005	Safety for Radiofrequency Radiation
ISO 10993	1995	2012	Biocompatibility of Medical Devices

* 2nd Edition

21 CFR § 890.5290

Shortwave diathermy.

(a) ***Shortwave diathermy for use in applying therapeutic deep heat for selected medical conditions*** -- (1) *Identification*. A shortwave diathermy for use in applying therapeutic deep heat for selected medical conditions is a device that applies to specific areas of the body electromagnetic energy in the radio frequency bands of 13 megahertz to 27.12 megahertz and that is intended to generate deep heat within body tissues for the treatment of selected medical conditions such as relief of pain, muscle spasms, and joint contractures, but not for the treatment of malignancies.

(2) *Classification*. Class II (performance standards).

(b) ***Shortwave diathermy for all other uses*** -- (1) *Identification*. A shortwave diathermy for all other uses except for the treatment of malignancies is a device that applies to the body electromagnetic energy in the radio frequency bands of 13 megahertz to 27.12 megahertz and that is intended for the treatment of medical conditions by means other than the generation of deep heat within body tissues as described in paragraph (a) of this section.

(2) *Classification*. Class III (premarket approval).

Section 890.5290(a)
Product Code IMJ

(a) *Shortwave diathermy for use in applying therapeutic deep heat for selected medical conditions*

(1) *Identification*. A shortwave diathermy for use in applying therapeutic deep heat for selected medical conditions is a device that applies to specific areas of the body electromagnetic energy in the radio frequency bands of 13 megahertz to 27.12 megahertz and that is intended to generate deep heat within body tissues for the treatment of selected medical conditions such as relief of pain, muscle spasms, and joint contractures, but not for the treatment of malignancies.

(2) *Classification*. Class II (performance standards).

Section 890.5290(b)
Product Code ILX

(b) Shortwave diathermy for all other uses

(1) *Identification.*

Shortwave diathermy for all other uses except for the treatment of malignancies is a device that applies to the body electromagnetic energy in the radio frequency bands of 13 megahertz to 27.12 megahertz and that is intended for the treatment of medical conditions by means other than the generation of deep-heat within body tissues as described in paragraph (a) of this section.

(2) *Classification*. Class III (premarket approval)

Proposed Revision to 890.5290

Nonthermal shortwave diathermy

(1) *Identification*.

Nonthermal shortwave diathermy is a device that applies to the body pulsed electromagnetic fields in the radio frequency bands of 13.56 megahertz or 27.12 megahertz and that is intended for adjunctive use in the palliative treatment of postoperative pain and edema in superficial soft tissue, by means other than the generation of deep-heat within body tissues.

(2) *Classification.* Class II (special controls).

Device Description

Coalition devices:

- Subset of product code ILX
- Radiofrequency - RF (“shortwave”) signal
- Operate at 27.12 MHz
- Apply electromagnetic fields to the body

Industry Coalition Devices

REGENESIS BIOMEDICAL

Provant

IVIVI THE TECHNOLOGY OF LIFE

SofPulse Torino II

Replexa (PMT850)

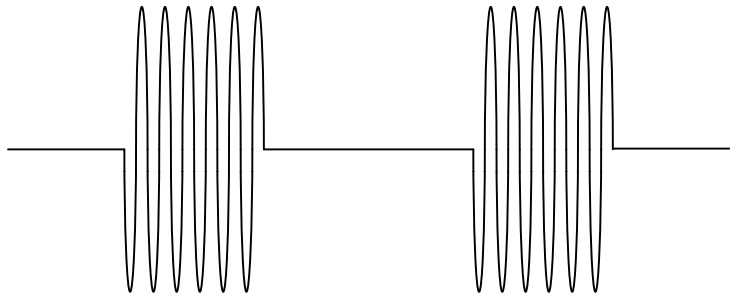
PROMEDTEK

OrthoCor Knee System

OrthoCor MEDICAL

Signal Characteristics

Pulse Modulation	
Carrier Signal	27.12 MHz
Pulse duration	0.04 – 2 msec
Repetition	2–1000 burst/sec
Duty Cycle	0.4 – 4.2%



Energy Density
0.12 – 0.14 $\mu Ws/cm^3$

Next Presenters

Professor Arthur Pilla

- Professor Biomedical Engineering, Columbia University
- Professor Emeritus, Department of Orthopedics, Mount Sinai School of Medicine
- Internationally recognized authority on electrotherapeutics

Richard Chiacchierini, PhD

- 20+ years at FDA
- Director of what is now the Division of Statistics in CDRH.
- Chief Scientist Officer in the Commissioned Corps of the United States Public Health Service

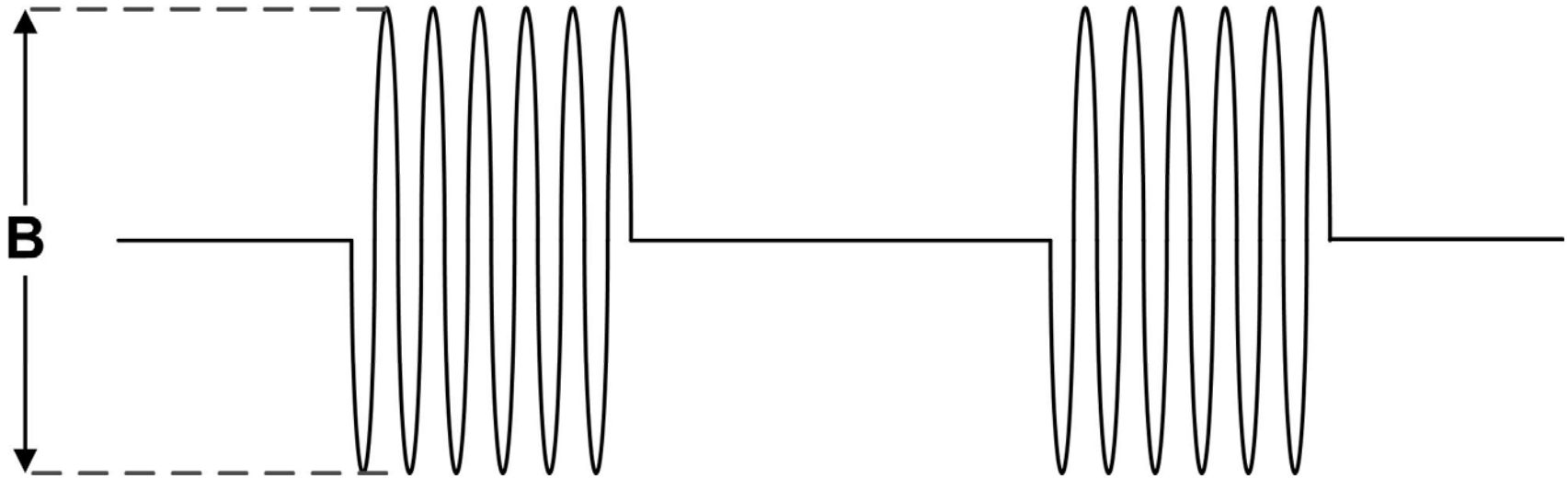
Industry Coalition Technology and Dosimetry

Arthur A. Pilla, PhD
Department of Biomedical Engineering, Columbia University, New York, NY
Department of Orthopedics, Mount Sinai School of Medicine, New York, NY
Senior Scientific Advisor to Ivivi Health Sciences, LLC

Technology and Dosimetry

- How we know the amount of RF energy Coalition devices deposit in tissue
- Evidence that a biologically effective dose can be defined from Energy Density
- Evidence that Coalition devices with different signal parameters deposit similar Energy Density and, therefore produce similar biological outcomes

Coalition Signal



Carrier: 27.12 MHz (ISM frequency - FCC defined)
Pulse duration: 0.04 - 2 msec
Duty Cycle: 0.4 – 4.2%
Peak Induced Magnetic Field (B): 2 - 200 μT

Energy Density is the dose

- *In situ* Energy Density can be calculated from induced electric field measurements (K070541)

  Energy Density = ***SAR × duty × pulse***

- Energy Density first accepted to define dose for 510(k) market clearance in 2008 (K070541)
- Subsequently accepted in 2009 (K091996, K092044), 2012 (K121338) and 2013 (K121702)

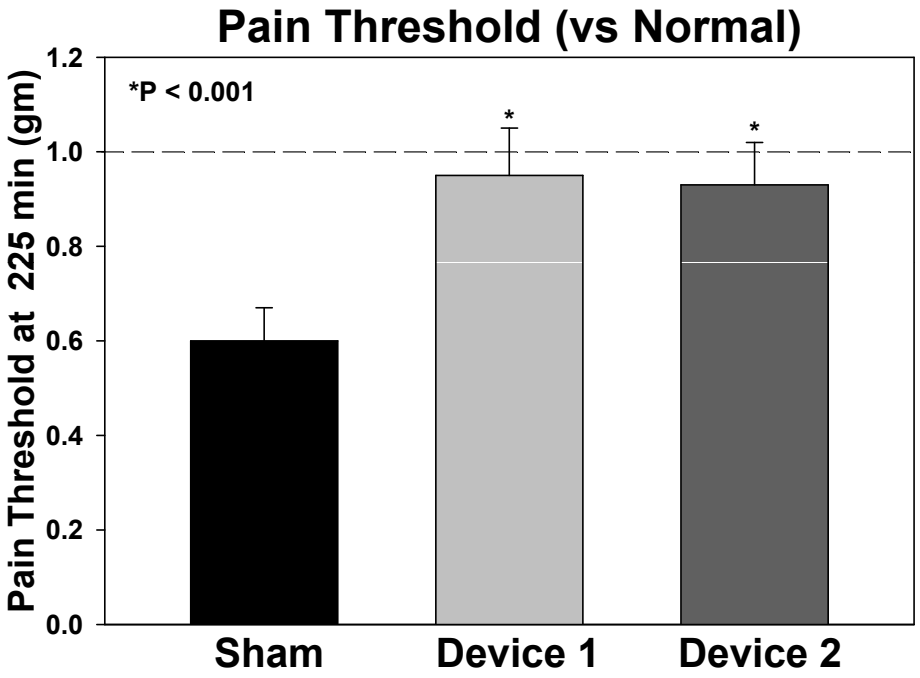
Coalition Device Dosimetry

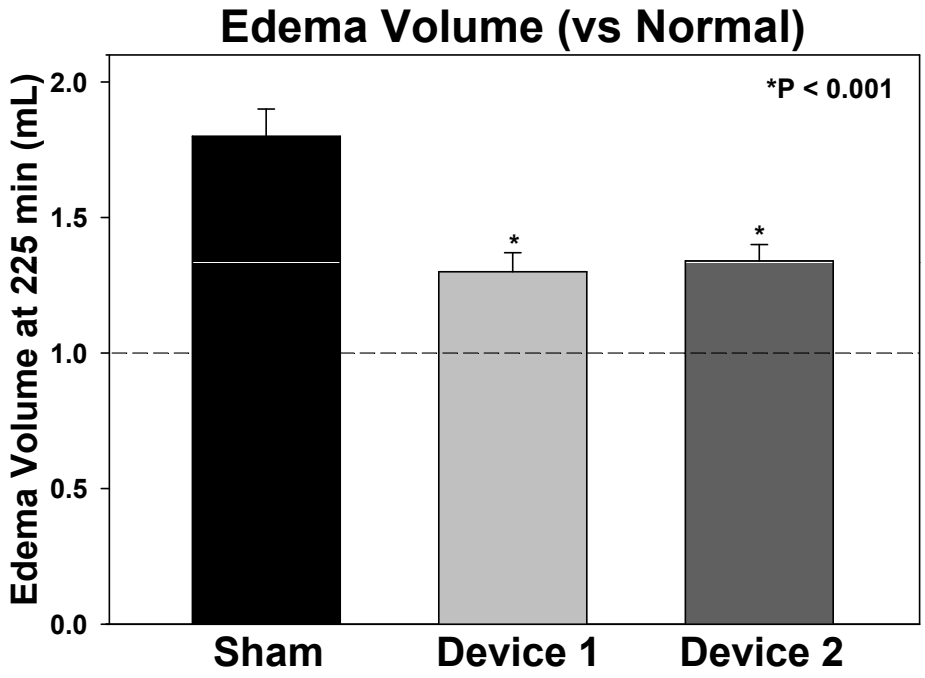
Energy Density (μWs/cm^3)							
MRT	912-M10	Roma^3	Provant	PMT850	OrthoCor Knee	Torino II	Zeobi
0.14	0.13	0.12	0.13	0.14	0.13	0.13	0.13

Coalition devices have different signal parameters

However, all deposit a similar Energy Density

Energy Density is Biologically Relevant





Evidence Requested and 510(k) cleared by FDA in 2008 (K070541)

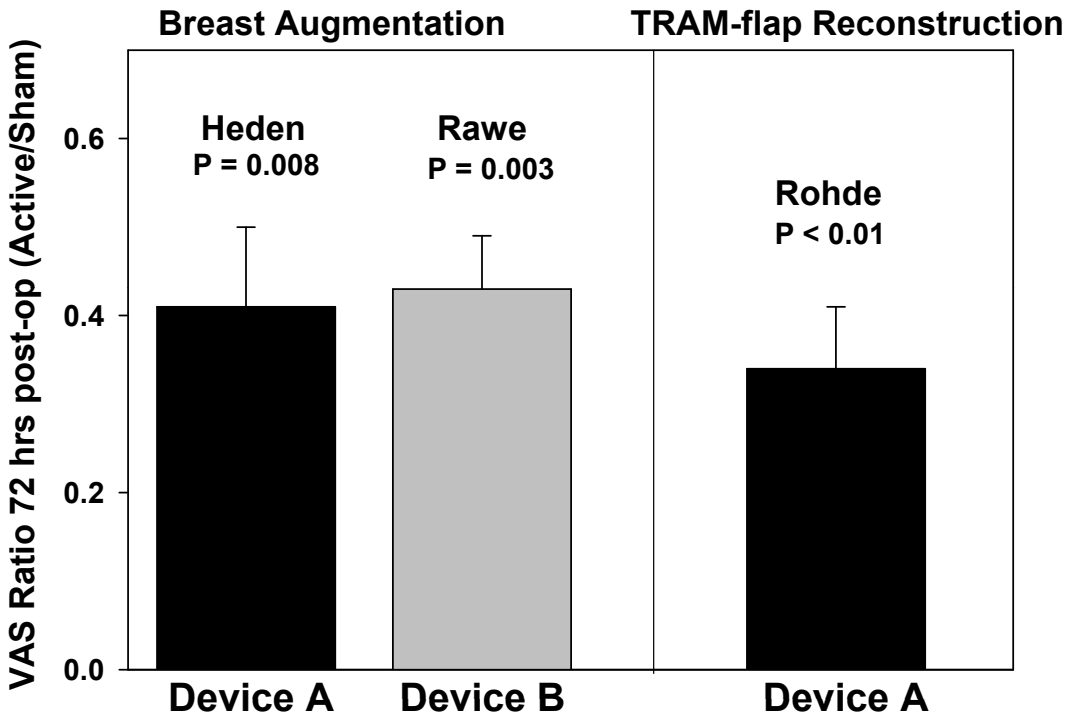
Carrageenan-induced hind paw inflammation in a blinded rat model

Devices with different signal parameters produce similar outcomes

Device 1: Energy Density = 0.14 $\mu Ws/cm^3$

Device 2: Energy Density = 0.13 $\mu Ws/cm^3$

Energy Density is Clinically Relevant



Post-op pain reduction in 3 randomized clinical studies

Devices with different signal parameters, but similar Energy Density reduce active cohort pain to < 50% of sham pain at 72 hrs post-op

Rohde et al. Plast Reconstr Surg. 2012;130(5S-1):91-92
Rawe et al. Aesthetic Plast Surg. 2012;36:458-463
Heden et al. Asthetic Plast Surg .2008;32:660-666

Summary

- Coalition devices deliver measurable RF energy to tissue (Energy Density)
- The *in situ* Energy Density, delivered by all Coalition devices is similar, despite substantial differences in signal parameters
- Energy Density can be used to define a biologically effective dose by which all Coalition devices can produce clinically meaningful effects on pain and edema
- Energy Density can serve as a special control

Valid Scientific Evidence of Effectiveness

Richard P. Chiacchierini, Ph.D.

President, R. P. Chiacchierini & Associates

Valid Scientific Evidence of Effectiveness

- There is a reasonable assurance of effectiveness in reducing post operative pain and edema in soft tissue
  - Extremely low probability that these results occurred by chance
  - Study size concerns mitigated by
    - Reproducibility of outcomes between studies
    - Different surgeries
    - Different study populations

Scientific Evidence of Effectiveness

- Level of Evidence
  - Level 1 – Eight randomized double-blind sham controlled clinical trials, six with good design and conduct
  - Level 2 – Three studies with concurrent controls that are either not randomized, not blinded, or neither
  - Level 3 – One Observational Study

Scientific Evidence of Effectiveness

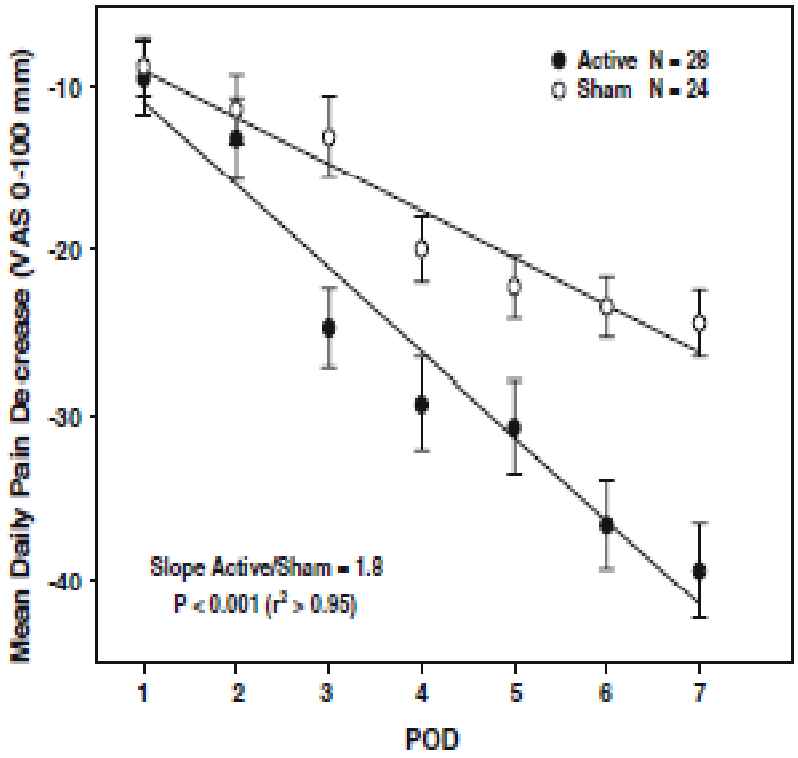
- 12 studies (9 studies support effectiveness and 3 show no effect)
- Only two adverse events were reported across all studies
- All but one Level 1 study have similar Energy Density ($\mu Ws/cm^3$)
- All measure postoperative pain, many also studied edema, and some ecchymosis or erythema

Common Features of Effective Level 1 Trials

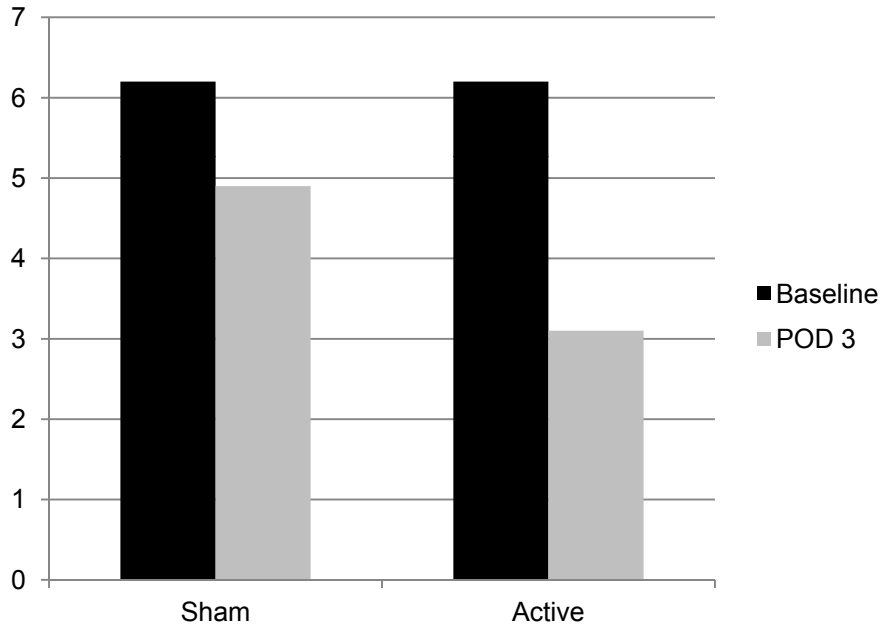
Authors	Randomized Double-Blind Sham-Controlled	Surgery	Energy Density ($\mu Ws/cm^3$)	Number of Patients	Endpoints
Hedén, Pilla (2008)	YES	Breast Augmentation	0.13	14 bilateral Active 14 bilateral Sham 14 contralateral	Pain 1 (VAS, 0-100), pill count, POD 0-7
Rohde et al. (2010)	YES	Breast Reduction	0.13	12 bilateral Active 12 bilateral sham	Pain (VAS, 0-10), edema Pill count, POD 0-2
Rohde et al. (2012)	YES	TRAM-flap Reconstruction	0.13	12 Active 11 Sham	Pain (VAS, 0-10), edema, pill count POD 0-3
Rawe et al. (2011)	YES	Breast Augmentation	0.12	8 bilateral Active 10 bilateral Sham	Pain (VAS, 0-10), pill count, POD 1-7
Kaplan, Weinstock (1968)	YES	Foot Surgery	0.15	100 foot surgery patients	Pain, edema, erythema (all 4 pt) POD 1-4
Bentall, Eckstein (1975)	YES	Orchidopexy	0.15	62 males paired by age and surgery side	Photodensitometry of wound & wound circumference

Hedén and Pilla Level 1 Results

Breast Augmentation



Pain

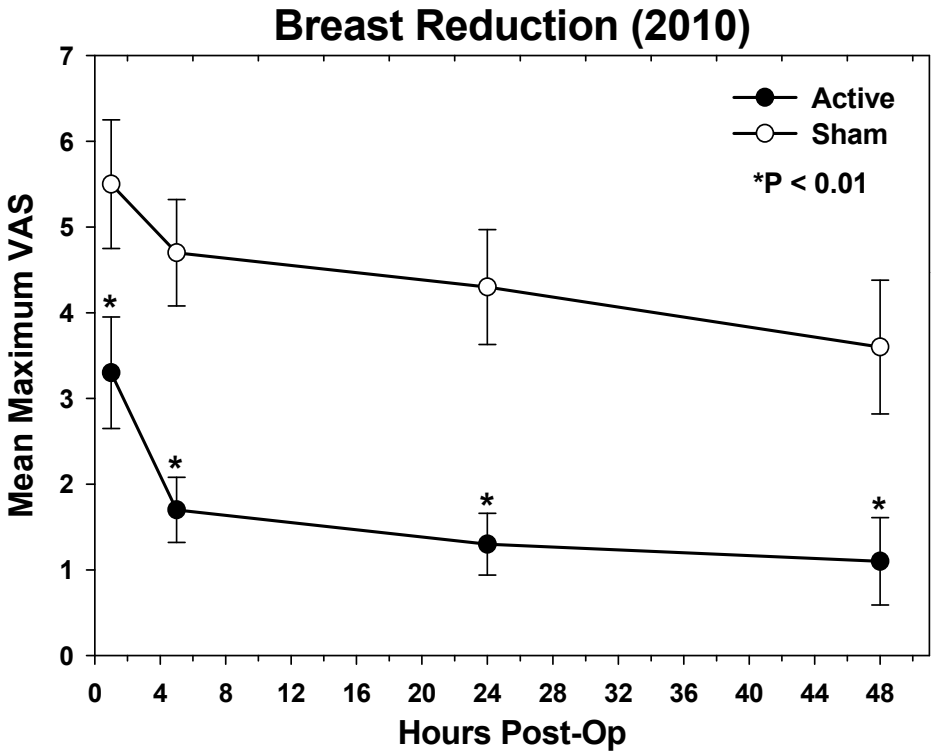


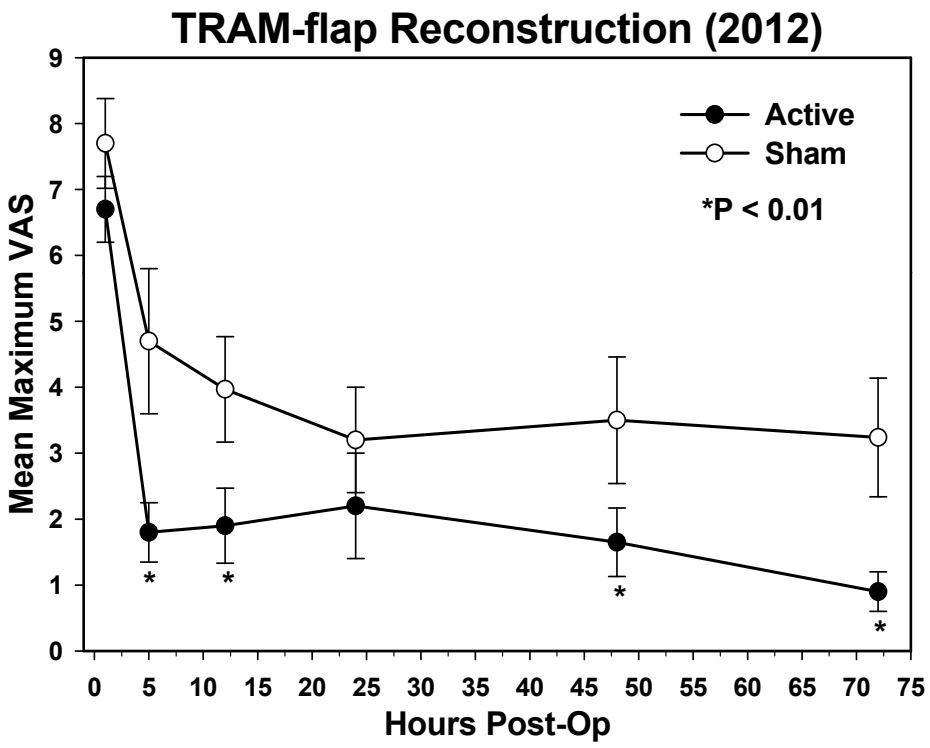
Percocet Equivalents

Active patients had a 2.9-fold greater reduction in medication use (P<0.001)

No adverse events observed

Rohde Level 1 Results: Post-op Pain

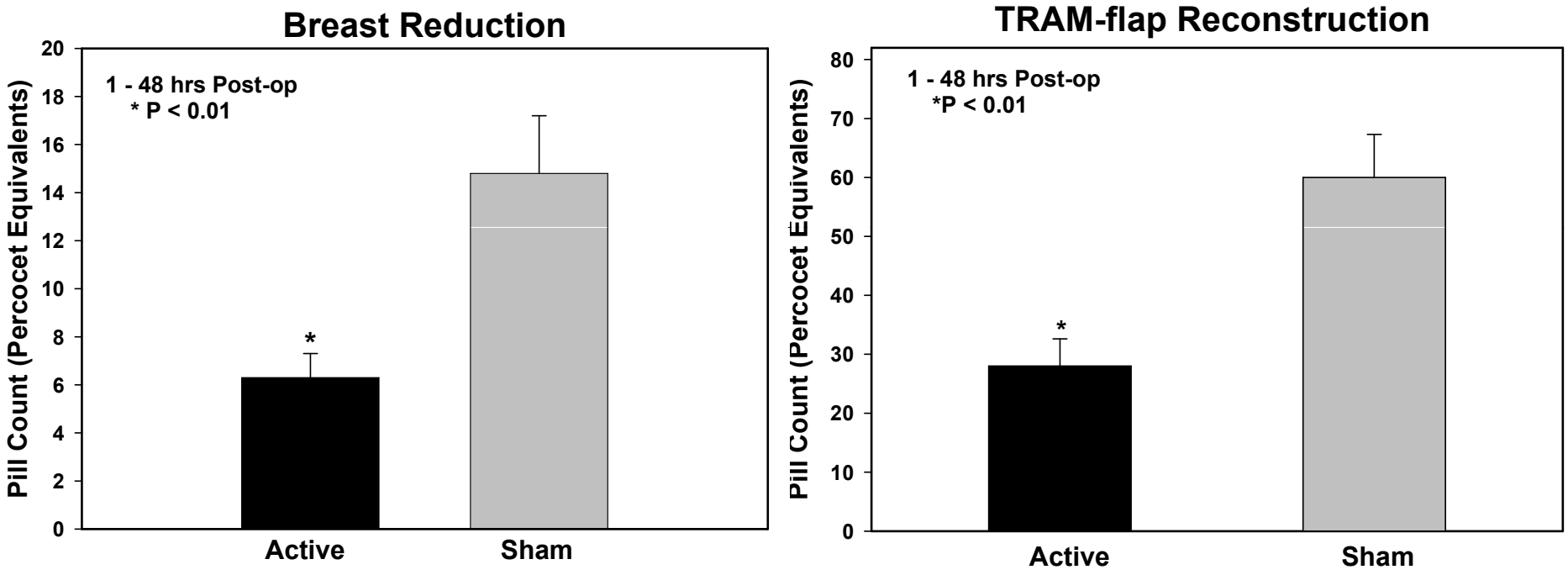




Exposure started in OR; No adverse events observed

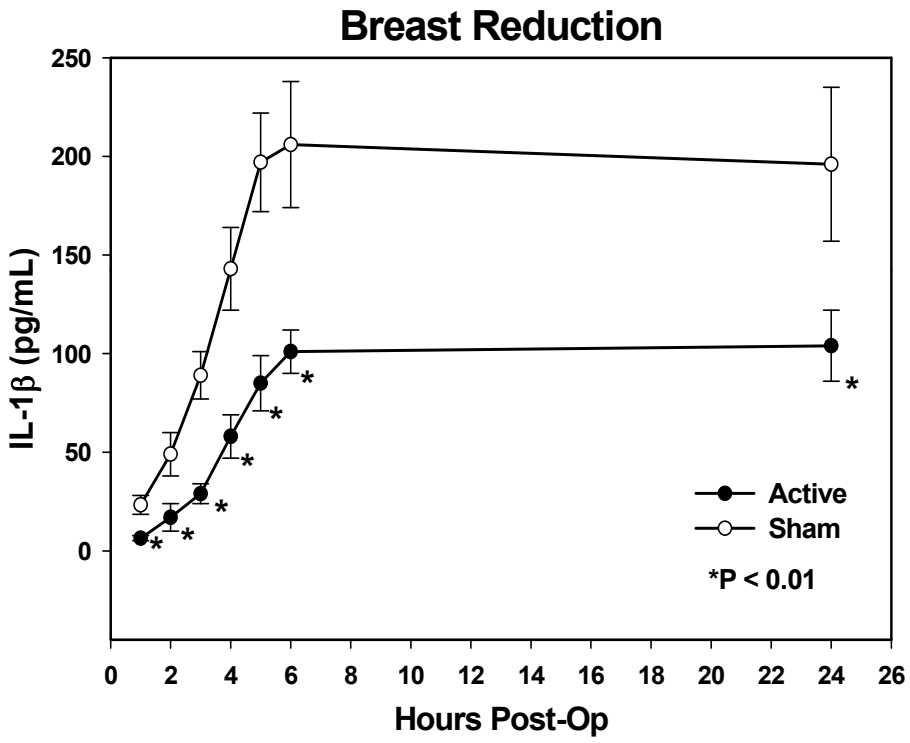
Pain reduction nearly 2-fold faster in active in first 5 hrs post-op. Pain at 48 – 72 hrs post-op > 3-fold higher in Sham cohort

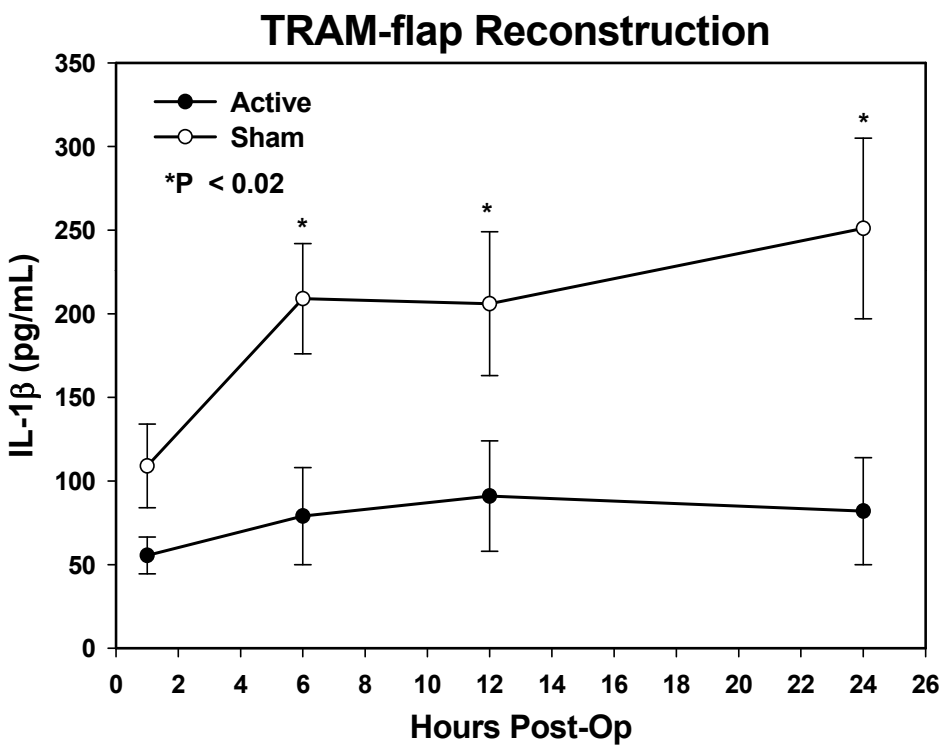
Rohde Level 1 Results: Post-op Narcotics



Sham patients required 2-fold more narcotic medication in first 48 hrs post-op (P < 0.01)

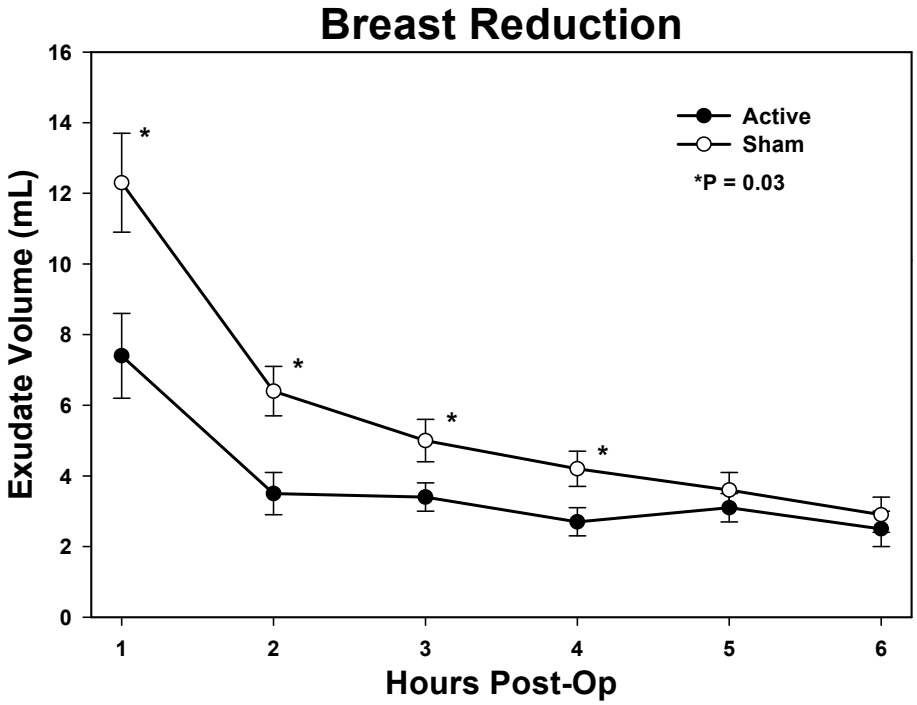
Rohde Level 1 Results: Post-op IL-1β

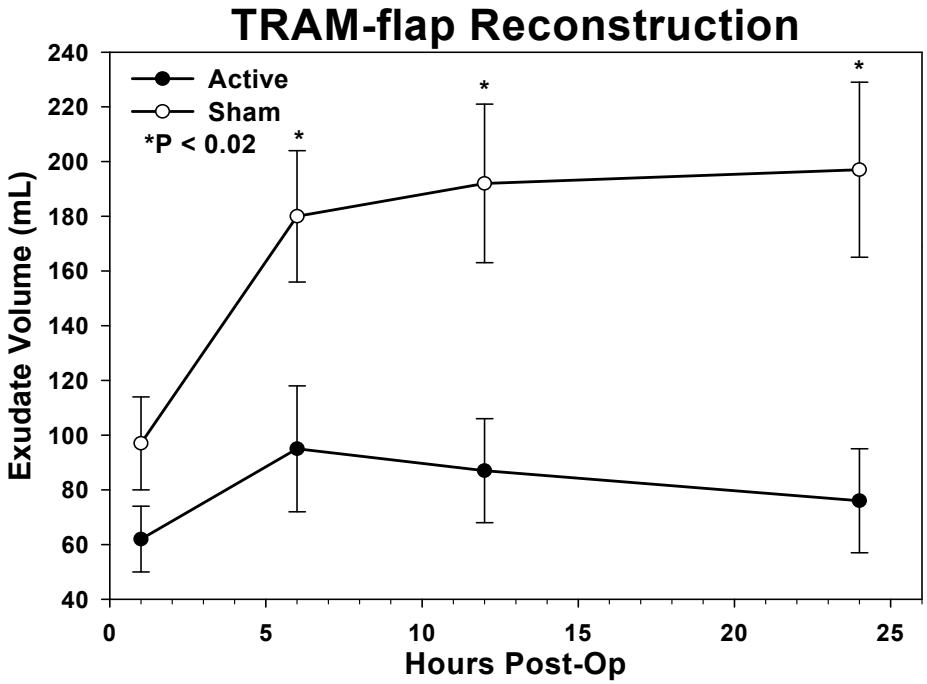




IL-1β 2 to 4-fold higher in sham exudate by 1 hr post-op

Rohde Level 1 Results: Exudate Volume

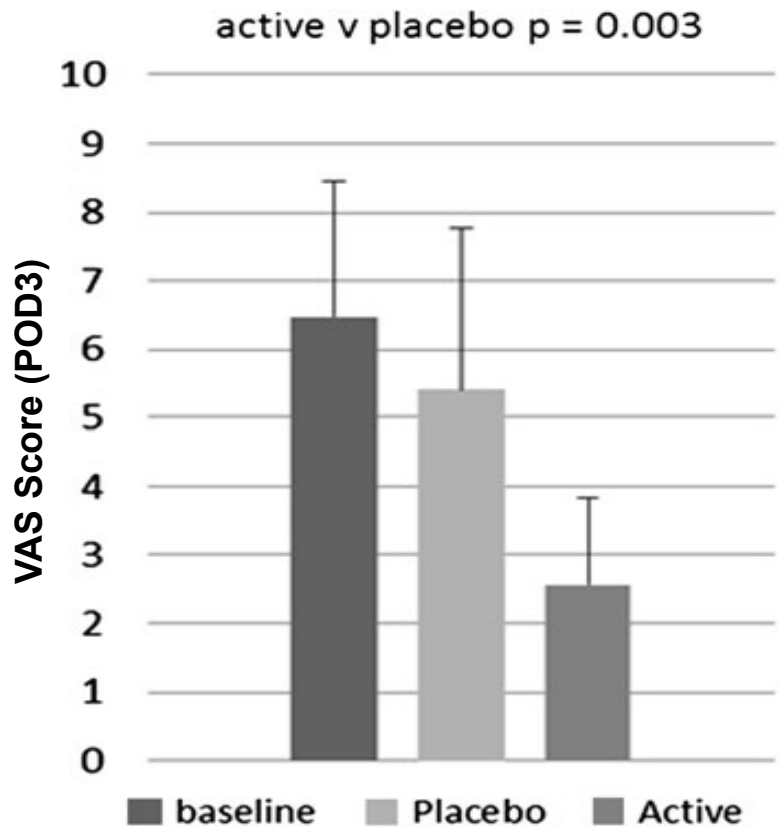




Exudate volume 2-fold larger in Shams within first 6 hrs post-op

Rawe et al. Level 1 Results

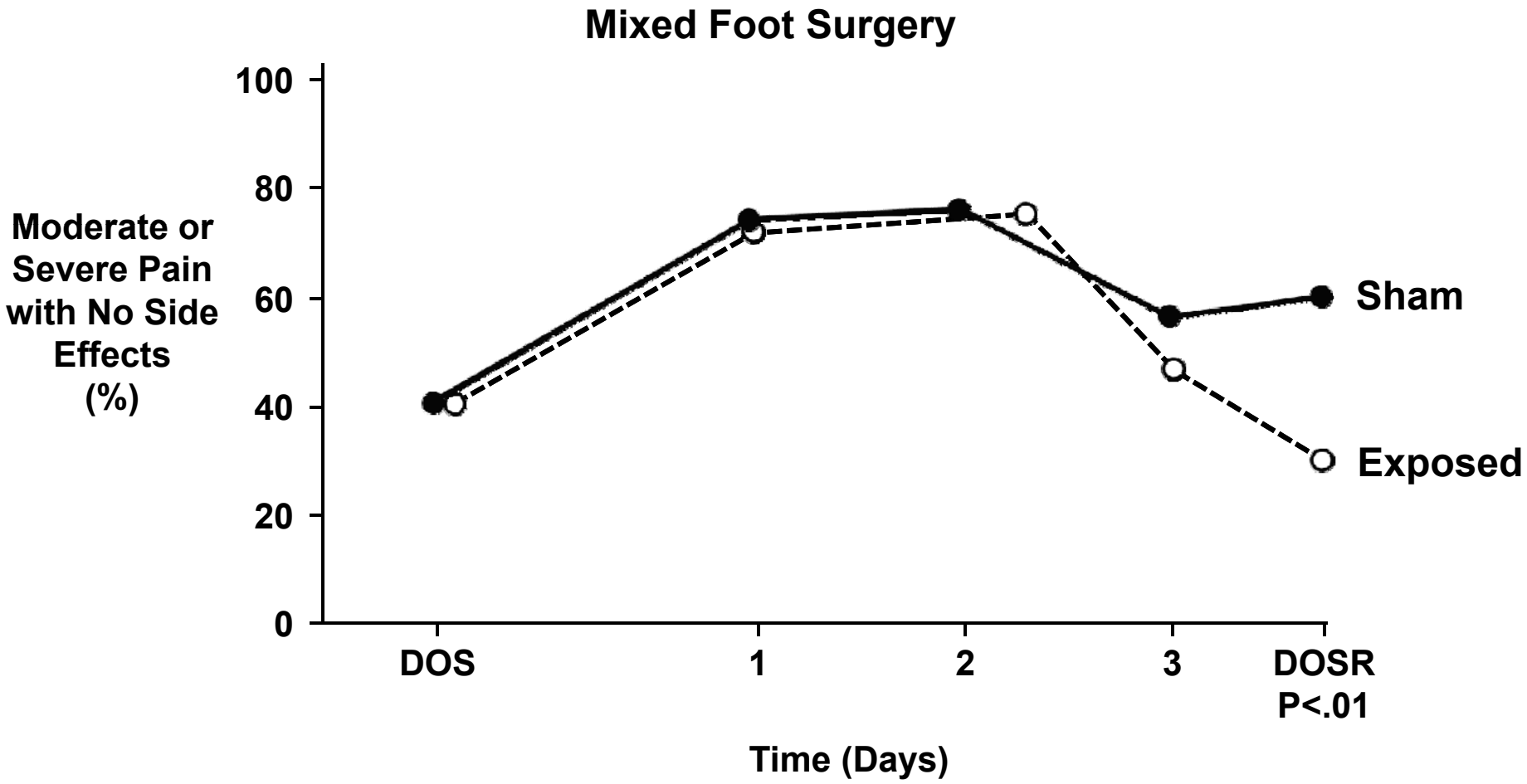
Breast Augmentation Postoperative Pain



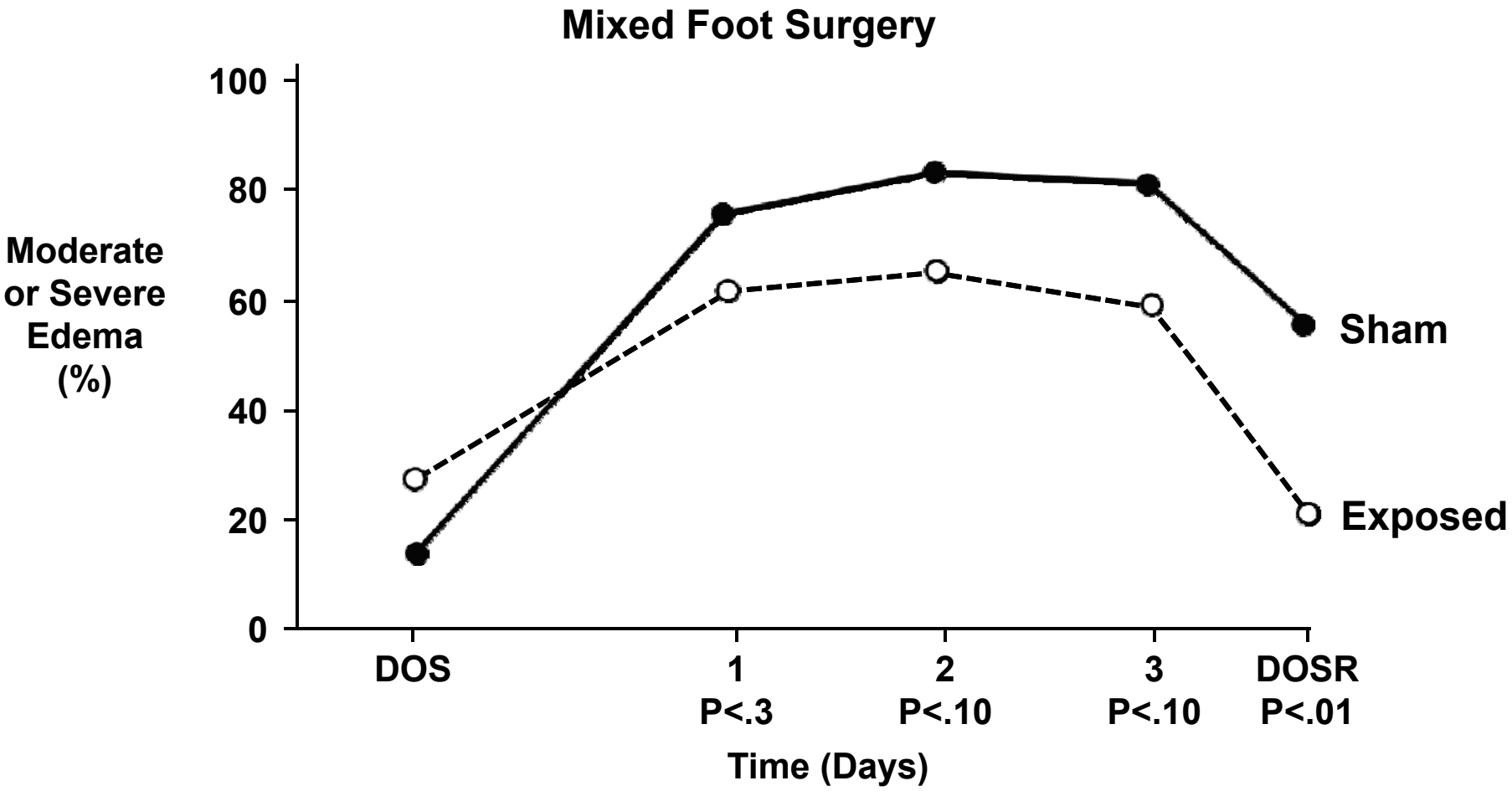
No adverse events observed

Pill count reduced in exposed group (P= 0.07) but one exposed patient was outlier taking 33 pills. Excluding this patient P=0.002.

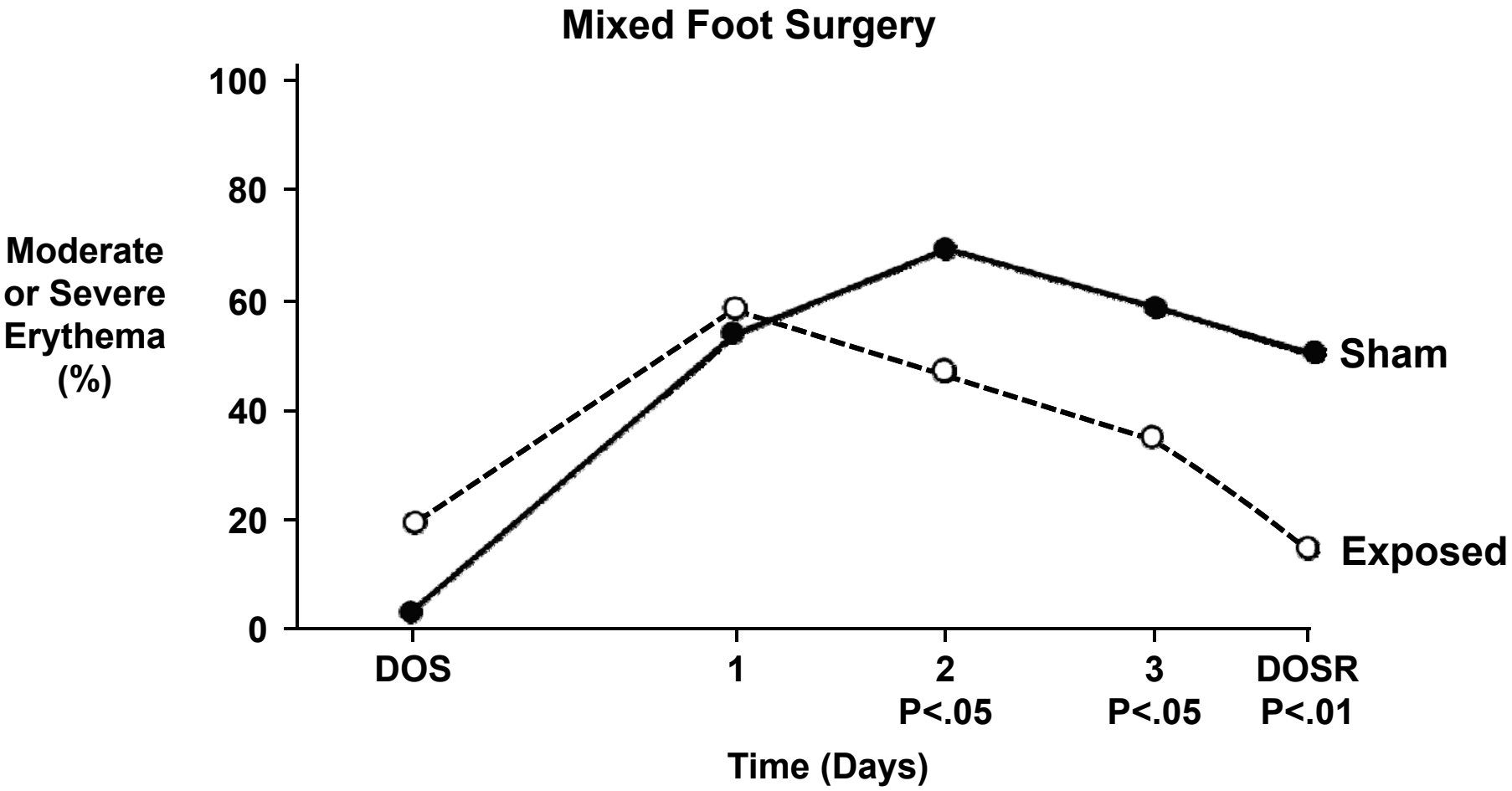
Kaplan and Weinstock Level 1 Results: Pain



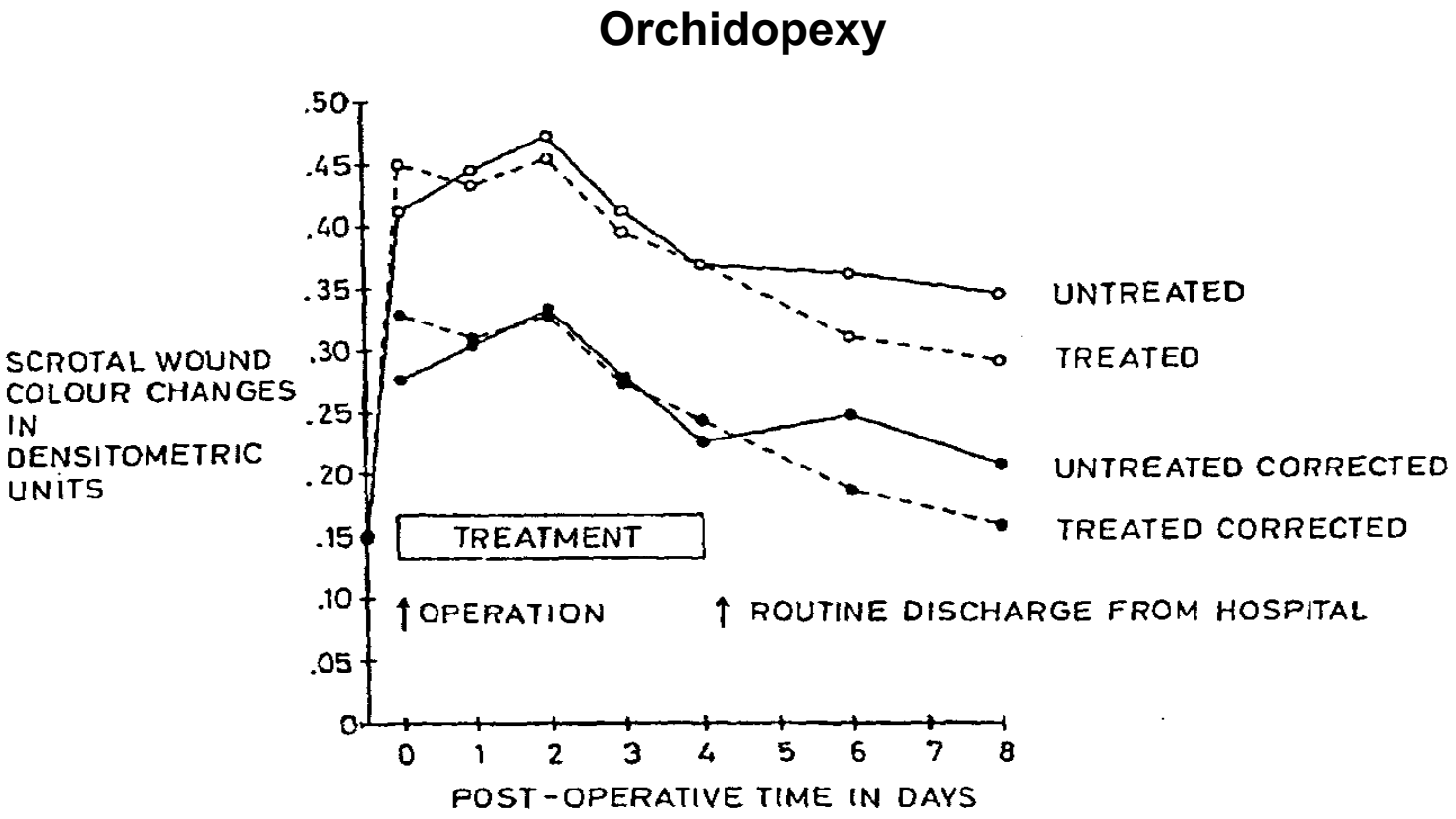
Kaplan and Weinstock Level 1 Results: Edema



Kaplan and Weinstock Level 1 Results: Erythema



Bentall and Eckstein Level 1 Results



Correction was for operative mobilization and difficulty. Wound circumference favored the exposed group but high variability prevented statistical significance. **No side effects seen.**

Level 1 No Effect Studies

Authors	Randomized Double-Blind Sham-Controlled	Surgery	Energy Density ($\mu Ws/cm^3$)	Number of Patients	Endpoints
Czyz et al. (2011)	YES	Blepharoplasty	0.11	54- Eyes randomized	Pain, edema, & ecchymosis
• Assessment time at POD 7 was too late (pilot study effects on POD 1-6) • Compliance with placement of device could not be confirmed (wear 7 hrs for 4.3 days) • Patients reported effect occurred prior to POD 7 • Two adverse events observed					
Reed et al. (1987)	YES	Inguinal Hernia	0.03	21 Active and 22 Sham	Independent Observer Pain Score
• Problem insufficient dose • Pain scores by independent observer not significant • No adverse events observed					

Level 2 Studies

Authors	Randomized Double-Blind Sham-Controlled	Surgery	Energy Density ($\mu Ws/cm^3$)	Number of Patients	Endpoints
Aronofsky (1971)	Neither	Oral	0.15	30 before and after 30 before 30 no exposure	Pain, inflammation, and effectiveness

• Statistically significant effects favor progressive active exposure
• Major problems:
  • Absence of sham exposure
  • Non-randomized allocation imbalanced dental procedures-cannot assure consistent pain levels					

Hutchison et al. (1978)	Double-blind not randomized	3rd Molar extraction	0.14	41 matched pairs	Pain by patient and swelling by surgeon
• Matching within operative day limits adequacy of match (age, sex, duration and day) • Surgeon evaluator not blinded and likely to severely bias assessments • Inconsistent assessments times (75% on POD 3, 25% on POD 5)					
Nicolle and Bentall (1982)	Uncertain	Blepharoplasty	0.10	21 Patients – eyes randomized	Edema and ecchymosis

• No statistical analysis of data presented (Pilot of Czyz et al. (2011))
  • 6 patients had too little edema and ecchymosis
  • 11 patients had better response on exposed side
• Benefit appeared on POD 1 and seemed to persist to POD 6					

Level 3 Study

Authors	Randomized Double-Blind Sham-Controlled	Surgery	Energy Density ($\mu Ws/cm^3$)	Number of Patients	Endpoints
Rhodes (1981)	Neither	Mixed oral	0.15	254 Controls 247 Active	Pain, edema, time in hospital, and time to return to work

- Non statistical analysis showed active patients stratified by gender and age showed lower pain, edema, time in hospital, and time to return to work than Sham
- Problems
  - Potential bias over time with possibly changing surgical procedures, hospital practices, and patient care (spans Medicare introduction in 1965)
  - Control group not a sham group
  - Author indicates that there were too many variables to control

Flawed Studies

- Poorly conducted Level 1 studies cannot provide evidence of lack of effectiveness
- Level 2 and 3 studies may contain biases that limit ability to provide evidence for or against effectiveness

Effectiveness Summary

Very strong evidence demonstrates effectiveness in multiple studies

- 4 studies involving soft tissue after different breast surgeries all showed pain significantly lower, each with small probability of Type I error
- Probability of a Type I error in all 4 independent trials in the same tissue is much, much smaller
- Minimizes the single site concern of the FDA and also extends to a broader treated population (generalizability)

Effectiveness Summary (cont.)

Very strong evidence demonstrates effectiveness in multiple studies

- Foot and orchidopexy surgery studies confirm a consistent effect in soft tissue
- Rohde studies using IL-1β and exudate volume endpoint confirm edema response
- Expands effectiveness to other populations and soft tissues Edema related measure of IL-1β supports edema subjective data

Effectiveness Conclusion

Valid scientific evidence exists on both effectiveness and safety “from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of the device under its conditions of use.”

Risks, Mitigation and Proposed Special Controls

Dr. Richard Isenberg

Vice President, Clinical and Regulatory Affairs

Regenesis Biomedical

Risks, Mitigation and Proposed Special Controls

- Risks are well understood, well characterized, infrequent and can be mitigated through special controls
- Special controls can provide a reasonable assurance of safety and effectiveness for the use and technologies described by the Coalition devices
- Devices can be safely regulated as Class II

Safety Profile is Favorable

- Decades of market experience
  - Few (6) MDRs
  - Complaint rate < 0.1%
- 2 adverse events in the on-label studies (Czyz)
  - Superficial burns associated with device tampering
- 2 other adverse events in 51 off/on-label studies
  - 2,313 subjects treated
    - Warmth (1)
    - Tingling(1)
  - Adverse event rate in the literature: 0.2% (confidence levels 0.0 to 0.4%)

International Agency Safety Reports

Publication	Year	Target	Conclusions
ANSI/IEEE C95.1-2005	2005	Review of 1300 articles	No nonthermal adverse health effects
European Commission: Scientific Support for Policies	2007	World Literature	No adverse biological effects
International Commission on Non-Ionizing Radiation Protection	2004 2009	World Epidemiology Literature	No adverse health effects
European Commission Scientific Committee on Emerging and Newly Identified Health Risks	2009	World Literature	No evidence of carcinogenesis, tumor promotion, teratogenicity

2012 Proposed Rule: Risks to Health

1. Cellular or Tissue Injury
2. Pacemaker Interference
3. Tissue Necrosis and Cutaneous Burns
4. Electrical Shock
5. Thermal Injury from Wires and Implants
6. Stray Radiation Hazard
7. Abnormal Cell Growth

2012 Proposed Rule: Risks to Health

1. ***Cellular or Tissue Injury***
2. Pacemaker Interference
3. Tissue Necrosis and Cutaneous Burns
4. ***Electrical Shock***
5. Thermal Injury from Wires and ***Implants***
6. ***Stray Radiation Hazard***
7. ***Abnormal Cell Growth***

Special Controls

- Special controls can be identified to mitigate each risk identified by FDA.
  - including those that are theoretical.

Risk of Cellular or Tissue Injury

- Literature Evidence of Risk: none
- MDR Adverse Events: none
- Complaints: none

Developments since 1979 Panel:

- Substantial consensus standards introduced

Risk of Cellular or Tissue Injury: Proposed Special Controls

Special Control	Risk Mitigation
ISO 10993: Biological Evaluation of Medical Devices	Testing for: Cytotoxicity Genotoxicity Immunotoxicity Carcinogenicity
FDA Guidance G95-1: Biocompatibility (new Draft Guidance 4/23/13)	
ANSI/IEEE C95.1-2005	SAR limits Exposure limits
IEC 60601-1 IEC 60601-2-3	Electrical Shock Mechanical Hazards
Clinical Testing	Actual use testing
Labeling	Long-term biological effects are unknown

Risk of Electrical Shock

- Literature Evidence of Risk: none
- MDR Adverse Events: none
- Complaints: none

Developments since 1979 Panel:

- Substantial international standards introduced

Risk of Electrical Shock: Proposed Special Controls

Special Control	Risk Mitigation
IEC 60601-1 IEC 60601-2-3	Electrical Shock protections and testing
IEC 60601-1-2	Electrostatic Discharge limits
Labeling (Precaution)	“Do not submerge”

Risk of Stray Radiation

Proposed Rule--FDA cited:

- Kloth 1984, Shields 2004, Martin 1990
- Each addresses *only* deep-heat diathermy

Developments since 1979 Panel:

- ICNIRP (2004, 2009): no evidence of risk occupational exposure, cancer, CV disease or cataracts in bystanders or operators

Risk of Stray Radiation: Proposed Special Controls

Special Control	Risk Mitigation
ANSI/IEEE C95.1-2005	Exposure limits
IEC 60601-1-2	Electromagnetic compatibility requirements
IEC 60601-1 IEC 60601-2-3	Requirements for shielding Stray Radiation limits
Labeling	Symbols and precaution

Risk of Abnormal Cell Growth

Proposed Rule--FDA cites:

- Frank (2002)
  - Benchtop study with already proliferating cells
  - Acceleration in normal on-going proliferation noted
  - No evidence of abnormal cell growth

Risk of Cellular or Tissue Injury: Proposed Special Controls

Special Control	Risk Mitigation
ISO 10993: Biological Evaluation of Medical Devices	Testing for: Cytotoxicity Genotoxicity Immunotoxicity Carcinogenicity
FDA Guidance G95-1: Biocompatibility (new Draft Guidance 4/23/13)	
ANSI/IEEE C95.1-2005	SAR limits Exposure limits
IEC 60601-1 IEC 60601-2-3	Electrical Shock Mechanical Hazards
Clinical Testing	Actual use testing
Labeling	Long-term biological effects are unknown

Risk of Pacemaker Interference

Literature Reports:

- From 1960s and 1970s
- Prior to introduction of pacemaker shielding
- No literature reports attributed to ILX devices per se

Risk of Pacemaker Interference

MDRs:

- 2007: Coalition device
  - Shock sensation and increased pacing
  - Resolved with cessation of treatment
- 1986: diathermy, unknown type
  - Increased pacing
  - Required reprogramming
- 1986: diathermy, unknown type
  - Stopped sensing
  - Required explanting

Risk of Pacemaker Interference: Proposed Special Controls

Special Control	Risk Mitigation
IEC 60601-1-2	Testing for: Interference Immunity
IEC 60601-1 IEC 60601-2-3	Electrical Shock
Labeling	Contraindicated Use by Patients with Pacemakers
Preclinical Testing	Simulated use tests for interference

Risk of Tissue Necrosis and Burns

Literature:

- Murray (2000) – increased perception of heat - Deep-heat device
- Erdman (1960) – increased surface temperature – Deep-heat device
- Czyz (2011) – superficial burns
  - Patients tampered with prototype devices
  - Removed insulation
  - Applied circuit board to skin

Risk of Tissue Necrosis and Burns

MDRs: not clearly attributed to ILX devices

- Superficial burn
  - Used with hot compress
- Blistering
  - Used with enzymatic debridement agent

Risk of Tissue Necrosis and Burns: Proposed Special Controls

Special Control	Risk Mitigation
ANSI/IEEE C95.1-2005	SAR limits Exposure limits
IEC 60601-1 IEC 60601-2-3	Testing for temperature rise Requirement for Isolation
Preclinical Testing	Simulated use testing
Clinical Information	Actual use reporting
Labeling	"Do not disassemble"

Risk of Implanted Devices with Wire Leads

Literature Reports:

2001

- 2 reports of thermal brain injury in patients with implanted neurostimulators
- Involved deep-heat diathermy devices
- FDA investigation
- Public health notification for all diathermy devices (2003)

Risk of Implanted Devices with Wire Leads

- Literature Evidence of Risk: none
- MDR Adverse Events: none
- Complaints: none

Risk of Metal Implants

- Literature:
  - No reports of this risk
  - Ruggera (Physics Med and Biol, 2003)
    - FDA investigation
    - < 1° C temp rise in tissue phantom

- MDR Adverse Events: none
- Complaints: none

Wire Leads and Metal Implants: Proposed Special Controls

Special Control	Risk Mitigation
ANSI/IEEE C95.1-2005	SAR limits Exposure limits
IEC 60601-1 IEC 60601-2-3	Testing for Temperature Rise
Labeling (warning)	Should not be used by Patients with Implanted Wire Leads
Preclinical Studies	Simulated Use Testing
Clinical Information	Actual use reporting

Risks to Health: 2012 Proposed Rule

1. Pacemaker Interference
2. Tissue Necrosis and Cutaneous Burns
3. Thermal Injury from Wires and Implants
4. Cellular or Tissue Injury
5. Electrical Shock
6. Abnormal Cell Growth
7. Stray Radiation Hazard

Risk in Pregnancy
Risk in Children

- Literature Evidence of Risk: none

  Recent international agency safety reviews (ICNIRP 2009, ANSI/IEEE C95.1-2005) identify no adverse pregnancy outcomes with shortwave RF therapy.

- MDR Adverse Events: none
- Complaints: none

Risk in Pregnancy and Children: Proposed Special Controls

Special Control	Risk Mitigation
ANSI/IEEE C95.1-2005	SAR limits Exposure limits
IEC 60601-1 IEC 60601-2-3	Electrical Safety
Labeling (precautions)	Not studied in pregnancy Not studied in children

Further FDA Proposed Risks

Complaint	Complaint/1,000 pts
Pain	0.6
Skin Reaction	0.1
Tingling/Pricking, Numbness, Bleeding, Warmth, Headache/Malaise, Ineffective Treatment, Skin cancer, Abdominal Pain, Burn, Chilliness, Gout attack, Chest wall sensation	<0.05

Risks of Pain and Skin Reaction: Proposed Special Controls

Special Control	Risk Mitigation
ISO 10993: Biological Evaluation of Medical Devices	Testing for: Cytotoxicity Genotoxicity Immunotoxicity Carcinogenicity
FDA Guidance G95-1: Biocompatibility (new Draft Guidance 4/23/13)	
ANSI/IEEE C95.1-2005	SAR limits Exposure limits
IEC 60601-1 IEC 60601-2-3	Electrical Shock Mechanical Hazards
Labeling	Do not apply directly to the skin

Overview: Proposed General and Special Controls

Risk	IEEE C95.1	Electrical Safety	EMC	Preclinical Analysis	Labeling	Biocomp.	Clinical Information	QSR
Pacemaker Interference		✓	✓	✓	✓			✓
Tissue Necrosis and Burns	✓	✓		✓	✓		✓	✓
Wire Leads	✓	✓		✓	✓		✓	✓
Adverse Pregnancy Outcome	✓	✓			✓			✓
Risks to Children	✓	✓			✓			✓
Pain	✓				✓			✓
Skin Reaction	✓	✓			✓	✓		✓

Proposed Special Controls Summary

- Each actual risk can be mitigated by multiple special and general controls
- Special controls have been identified that reasonably assure device safety and effectiveness as a Class II device
- Statutory Requirements for Class II are met and devices within the industry coalition type should thus be reclassified

Conclusion

Dr. Richard Isenberg

Industry Coalition ILX Devices

K Number	Year	Product	Manufacturer
K903675	1991	MRT SofPulse	Ivivi Health Sciences
K070541	2008	SofPulse 912-M10	
K070541	2008	SofPulse Roma^3	
K070541	2008	SofPulse Torino II	
K121388	2012	Zeobi	
K972093	1997	Provant Model 42	Regenesis Biomedical
K091791	2010	Provant System Model 4201	
K070931	2007	Model PMT850	ProMedTek
K091996	2009	Orthocor Knee System, Basic	Orthocor Medical
K092044	2009	Orthocor Knee System, XL	
K121702	2013	Orthocor, Active Device	

INDICATION

Adjunctive use in the palliative treatment of post-operative pain and edema in superficial soft tissue

Coalition Devices Deliver Uniform Dose

All Coalition devices deliver the same clinically meaningful dose to target tissues

Energy Density (μWs/cm^3)							
MRT	912-M10	Roma^3	Provant	PMT850	OrthoCor Knee	Torino II	Zeobi
0.14	0.13	0.12	0.13	0.14	0.13	0.13	0.13

Valid Scientific Evidence

Authors	Randomized Double-Blind Sham-Controlled	Surgery	Endpoints	P value
Hedén and Pilla (2008)	YES	Breast Augmentation	Pain, pill count	P<0.001
Rhode et al. (2010)	YES	Breast Reduction	Pain, pill count, exudate volume, IL-1β	P≤0.03
Rhode et al. (2012)	YES	TRAM-flap Reconstruction	Pain, pill count, exudate volume, IL-1β	P<0.02
Rawe et al. (2011)	YES	Breast Augmentation	Pain, pill count	P=0.002*
Kaplan and Weinstock (1968)	YES	Foot Surgery	Pain, swelling and erythema	P<0.01
Bentall and Eckstein (1975)	YES	Orchidopexy	Photodensitometry of photo of wound and wound circumference	P<0.05

* Pill count reduced in exposed group (P=0.07) but one exposed patient was outlier taking 33 pills. Excluding this patient P=0.002.

Proposed General and Special Controls

Risk	IEEE C95.1	Electrical Safety	EMC	Preclinical Analysis	Labeling	Biocomp.	Clinical Information	QSR
Pacemaker Interference		✓	✓	✓	✓			✓
Tissue Necrosis and Burns	✓	✓		✓	✓		✓	✓
Wire Leads	✓	✓		✓	✓		✓	✓
Adverse Pregnancy Outcome	✓	✓			✓			✓
Risks to Children	✓	✓			✓			✓
Pain	✓				✓			✓
Skin Reaction	✓	✓			✓	✓		✓

Proposed Revision to 21 CFR 890.5290

Nonthermal shortwave diathermy

(1) *Identification*.

Nonthermal shortwave diathermy is a device that applies to the body pulsed electromagnetic fields in the radio frequency bands of 13.56 megahertz or 27.12 megahertz and that is intended for adjunctive use in the palliative treatment of postoperative pain and edema in superficial soft tissue, by means other than the generation of deep-heat within body tissues.

(2) *Classification.* **Class II (special controls).**

Conclusion

Statutory Criteria for Class II Classification

Special controls together with general controls provide reasonable assurance of safety and effectiveness of the device.

(Food, Drug, & Cosmetic Act)

All Statutory and Regulatory criteria for reclassification of coalition-type devices to Class II are met.